III. REMARKS

Claims 1 to 40 are pending in the subject application. Claims 24 to 40 have been withdrawn from consideration as a result of a requirement for restriction. Claims 1 to 23 were examined and stand variously rejected.

Claims 1-7, 13-16, 21 and 22 have been amended. Support for the amendments to these claims is found in the application papers as originally filed. Thus, the amendments do not raise an issue of new matter and entry thereof is respectfully requested.

In view of the preceding amendments and the remarks that follow, reconsideration and withdrawal of the rejections of the claims is respectfully requested.

35 U.S.C. § 112, Second Paragraph

Claims 4-9, 14-16, 22 and 23 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Office alleged that claim 4 is confusing in the recitation "said selection marker is leucine, histidine, tryptophan, or uracil" as leucine, histidine, tryptophan, and uracil can not be comprised within a vector.

The Office also noted that claims 5 and 6 are confusing in the recitation of "said expression vectors contain a tag" and "said tag is myc, HA, or FLAG 6his" as vectors cannot comprise peptide tags. The Office further noted that the "or" in claim 6 should be correctly placed following the word "FLAG".

The Office stated that claim 7 (upon which claims 8 and 9 depend) is confusing in the recitation of "said yeast expression vectors contain an inducible promoter or a constitutive promoter" as the vectors are limited in claim 1 (from which Claims 7-9 depend) to comprising inducible promoters. Claim 14 allegedly antecedent basis for "said IKKa" in claim 11 and "said IKKB" in claim 10. Claim 15 allegedly lacks antecedent basis for "said leu(met) vector". Claim 16 allegedly is confusing in the recitation "wherein constitutive expression is induced under the

alcohol dehydrogenase promoter" as the vectors are limited in claim 1 (from which Claim 16 depends) to comprising inducible promoters.

Claim 22 and 23 were objected to for allegedly lacking antecedent basis for "said purified IKK protein".

Claim 22 was objected to for use of the term "substantially homologous to IKK isolated from wild-type cells" on the ground that the term "substantially homologous" is a relative term which renders the claim indefinite. Furthermore, the Office argued that claim does not define what cells are the "wild-type" cells such that a skilled artisan would even know what the reference protein is.

Without conceding the correctness of the Office's position, the claims have been amended in a sincere effort to overcome the grounds for rejection. In view of these amendments, reconsideration and withdrawal of the rejections of the claims under 35 U.S.C. § 112, second paragraph is respectfully requested.

35 U.S.C. § 112, First Paragraph

Claims 14-16 stand rejected under 35 U.S.C. § 112, first paragraph on the ground the claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Office noted that claims 14-16 recite two specific vectors for which the specification and prior art are alleged to fail to provide a sufficient description of, i.e., pES 86(+) and leu(met). The Office acknowledged that pages 13-14 of the specification imply that these vectors are commercially available from Stratagene, but the Stratagene web site and online catalog did not contain mention of these vectors. The Office also stated that the specification includes no description of the components of these vectors such that one can know how they differ from any other yeast expression vectors. The Office stated that for purposes of further examination, the phrase "a met promoter from a leu(met) vector" in claim 14 is interpreted as any promoter that is repressed in the presence of methionine and induced by the removal of methionine, the phrase

"subcloned into said leu(met) vector" in claim 15 is interpreted as subcloned into any yeast expression vector comprising a promoter that is repressed in the presence of methionine and induced by the removal of methionine and the phrase "subcloned into the pES 86(+) vector" in claim 16 is interpreted as subcloned into any yeast expression vector comprising a alcohol dehydrogenase promoter.

Claims 14-16 were further rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the enablement requirement.

The Office stated that the invention appears to employ novel vectors, i.e., pES 86(+) and leu(met), that appear to be essential to the claimed invention, and so they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The Office alleged that the claimed plasmids' sequences are not fully disclosed, nor have all the sequences required for their construction been shown to be publicly known and freely available. The Office stated that the enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the plasmids.

Applicants respectfully traverse for the reasons which follow.

Applicants have amended the claims to more particularly point out that the parental expression vectors are the Stratagene vectors pESC. Stratagene currently sells these vectors as shown on the attached print-out from the company's web site. In addition, the specification has been amended to correct the typographical error appearing on page 13, line 27. Accordingly, the parental vectors, which are only exemplary of a number of suitable expression vectors, are commercially available. Accordingly, in view of the preceding amendments and remarks, reconsideration and withdrawal of the rejections are respectfully requested.

35 U.S.C. § 103

Claims 1-13, 16-20, and 22-23 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over either Li et al. or Rothwarf et al. in view of Epinat et al.

The Office argued that each of Li et al. and Rothwarf et al. teach the coexpression of IKKa, IKKB and IKKy genes in a eukaryotic host by inserting the genes encoding each subunit fused to a tag (HA, FLAG or c-myc) into a mammalian expression vector, growing the host cell, lysing the host cell, and immunoprecipatating the IKK complexes. The Office opined that the only difference in the methods taught by Li et al. and Rothwarf et al. to the methods of the instant claims is that in the instant claims the expression host used is yeast.

Epinat et al. also is alleged to teach that yeast is a convenient host for the reconstitution of the NF-kB system since it does not contain any indogenous NF-kB activity and that the reconstituted system provides an easy assay for testing stimuli or specific proteins that are postulated to be involved in NF-kB signaling. Epinat et al. is further alleged to teach expression vectors for the recombinant expression of genes involved in the NF-kB signaling pathway in yeast cells under the control of both constitutive promoters such as the ADH1 promoter and inducible promoters such as the GAL1 promoter, and that the yeast expression vectors comprise selection markers such as the URA3 or LEU2 genes.

The Office opined that as the IKK complex is well known to be part of the NF-kB signaling pathway, it would have been obvious to one of ordinary skill in the art to reconstitute the IKK complex in a yeast host cells by expressing the IKK subunit genes of Li et al. or Rothwarf et al. in yeast using any known yeast expression vector or yeast expression vectors as taught by Epinat et al.

Claims 14, 15, and 21 also stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Li et al or Rothwarf et al. in view of Epinat et al., as applied to claims 1-13, 126-20, and 22-23 above, and further in view of either or both of Mumberg et al. or page 23 of the 1999 Stratagene catalog.

The Office argued that Li et al., Rothwarf et al. and Epinat et al. teach as discussed supra, but acknowledged that they do not teach the specific yeast expression vectors recited in the instant claims.

Mumberg et al. was cited for teaching yeast expression vectors which include a methionine repressible promoter which is inducible by growing the yeast cells in media lacking methionine.

Page 23 of the 1999 Stratagene catalog was cited for teaching the pESC yeast expression vectors which designed for expression and functional analysis of eukaryotic genes in yeast and specifically designed to provide epitope tagging of the expressed proteins.

The Office stated that therefore, as each Mumberg et al. and the Stratagene catalog teach vectors specifically designed for the expression of heterologous genes in yeast it would have been obvious to use these vectors, or a vector including the methionine repressible promoter of Mumberg et al. and the epitope tagging and other features of the pESC vectors for the expression of the genes of Li et al. or Rothwarf et al.

Applicants respectfully traverse. The pending claims are directed to methods for reconstituting IKK in a yeast expression system. Applicants' method can produce IKK complexes with biological activity comparable if not identical to native or wild-type IKK complex.

Li et al. discloses expression of IKKα with either IKKα or IKKβ in a mammalian cell system. As Applicants' note in the instant specification, "because IKK is a large complex composed of three different subunits, there may be multiple complexes of IKK which exist to respond to different signals. Furthermore, IKK responds to over 150 signals, studying IKK in mammalian cells is particularly difficult." See page 4, line 30 to page 5, line 2 of Applicants' specification. Indeed, Li et al. was able to only transiently transport and express mammalian cells. See page 4498, right column, second paragraph under the "Discussion" section.

Similarly, Rothwarf et al. discloses transient expression and isolation of IKK subunits in mammalian cells. Rothwarf et al. does not teach or suggest that complete IKK complex can be reconstituted in a yeast expression system.

Epinat et al. teaches the transient expression of a p105 precursor of the p50 subunit of NF-kB. Thus, Epinat et al. at best teaches the expression of a precursor protein. The authors

attempted to reconstitute the complete IKK complex but were unsuccessful because they did not yet have the identity or the sequences of the individual subunits necessary for recombinant expression. Instead, Epinat et al. reconstituted kβ/Ikβα, which is the downstream target of IKK. The addition of Mumberg et al. or the Stratagene catalog fail to overcome the deficiencies in the prior art and fail to rebut the teaching of Epinat et al. that functional IKK expression in yeast was not possible. Thus, the combination of Li et al., Rothwarf et al., Epinat et al., Mumberg et al. or Stratagene, fail to teach or suggest the claimed invention. Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103.

IV. CONCLUSION

If a telephone interview would advance prosecution of the subject application, the Examiner is invited to telephone the undersigned at the number provided below. In the unlikely event that the transmittal letter is separated from this document and/or the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 50-2518** referencing billing reference 7004234002. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Date: April 19, 2005

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